ORIGINAL ARTICLE

Quality of Sleep and Related Factors During Chemotherapy in Patients with Stage I/II Breast Cancer

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Background: Insomnia causes severe distress in patients with breast cancer who receive chemotherapy. Few studies have focused on using objective methods to assess sleep. This study explored the quality of sleep and related factors in patients with breast cancer during chemotherapy.

Methods: The participants were 16 women with stage I or II breast cancer receiving their third cycle of chemotherapy with cyclophosphamide, epirubicin and fluorouracil, or cyclophosphamide, methotrexate and fluorouracil. The effects of chemotherapy on sleep were assessed on the 8th and 9th days of the third cycle, i.e. the active phase in terms of side effects, and the last 2 days before the start of the fourth cycle for comparison. Instruments used to assess sleep quality and related factors included actigraphy, the Hospital Anxiety and Depression Scale (HADS), the Symptom Distress Scale (SDS), the Fatigue Visual Analogue Scale (FVAS), the Epworth Sleepiness Scale (ESS), and sleep logs.

Results: During the active phase, patients showed an anxiety tendency with an average HADS score of 7.8 ± 3.8. The average FVAS score was 4 ± 2, indicative of mild fatigue, and SDS score (1.8 ± 0.3) also indicated mild symptom distress. The number of awakenings each night was 2.2 ± 1.6 by sleep logs, and the total time spent awake during these episodes was 47.8 ± 26.1 minutes by Actiwatch. Sleep efficiency measured by Actiwatch in the active phase was 82.1 ± 9.4% below the normal limit. Daytime sleepiness assessed by ESS showed mild sleepiness (6.0 ± 3.5) in the active phase.

Conclusion: The study showed poor sleep quality and daytime sleepiness in patients with breast cancer during the active phase of chemotherapy. Chemotherapy may bring symptom distress to patients and adversely influence sleep quality. [*J Formos Med Assoc* 2006;105(1):64–69]

Key Words: actigraphy, breast cancer, chemotherapy, sleep quality

Chemotherapy is one of the main treatments for breast cancer. Insomnia causes severe distress in patients with cancer who receive chemotherapy.[1] Sleep disturbances not only induce discomfort in patients and interfere with their daily activities, but also adversely influence their will to receive treatment and, consequently, treatment outcome. There have been few studies of sleep quality in patients with breast cancer receiving chemotherapy. Berger and Higginbotham found that total sleep time and sleep latency were increased during chemotherapy in patients with breast cancer, but their sleep efficiency was still normal.[2] Piper reported that prolonged total sleep time, difficulty in falling asleep, and frequent sleep interruptions and insomnia in patients receiving chemotherapy made it difficult for them to obtain good sleep quality.[3] Other factors such as anxiety, depression, fatigue, symptom

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distress, environment, age, education, marital status and menstruation could also influence sleep quality. Insomnia is highly correlated with the severity of anxiety and depression.[4–6] A high degree of anxiety and depression would increase sleep latency and make it difficult to fall asleep.[7–9] A high degree of fatigue would result in poor daytime function.[10]

Conventional sleep studies have mostly assessed sleep quality with subjective questionnaires and lacked objective data. Polysomnography is the standard measure for objective sleep assessment but it has some limitations, especially when used to assess insomnia.[11,12] For example, it can only be performed in a sleep laboratory where the unfamiliar environment is likely to adversely influence natural sleep. It also has a very high cost which may limit repeated measurements. Actiwatch (Cambridge Neurotechnology Ltd, Cambridge, UK) is a noninvasive device to monitor physical activity. Data recorded by Actiwatch can be transformed into sleep parameters.[13–15] Some studies indicated high correlation between actigraphy and polysomnography (r = 0.85–0.95).[13,16] This study used both subjective questionnaires and Actiwatch to assess sleep quality and related factors in patients with breast cancer during chemotherapy.

Methods

A prospective, descriptive, and repeated measures method was used in this study. The first period of data collection was during the 8th and 9th days of the third cycle of adjuvant chemotherapy, which was defined as the active period because both acute and delayed side effects are known to be most frequent and prominent during this period. The second period of data collection was 2 days before the fourth cycle of adjuvant chemotherapy, which was defined as the recovery period because most of the side effects from chemotherapy generally improve during this period. Both subjective and objective data from the two periods were compared.

Subjects

Female patients with stage I or II breast cancer receiving either a regimen of cyclophosphamide, epirubicin and fluorouracil (CEF) or cyclophosphamide, methotrexate and fluorouracil (CMF) were included. Both groups were in their third cycle of adjuvant chemotherapy. Subjects were between 18 and 65 years old, and were recruited from oncology clinics, general surgery clinics and the chemotherapy rooms of two medical centers. Patients with psychiatric or neurologic diseases that could cause sleep problems or result in tremor or limb paralysis were excluded.

Questionnaires

Hospital Anxiety and Depression Scale (HADS)

The HADS, developed by Zigmond and Snaith in 1983, is used to assess the degree of anxiety and depression of general medicine outpatients. A higher total score indicates a higher degree of anxiety or depression. The Chinese version of the HADS, authorized by the Nfer-Nelson company, was used in this study. Chen et al used the Chinese version of the HADS in a study of 90 cancer patients, and found that Cronbach's α for the degree of anxiety and degree of depression was 0.82 and 0.77, respectively, indicating the validity and reliability of the instrument.[17]

Fatigue Visual Analogue Scale (FVAS)

The subjective degree of fatigue of patients was measured on a 10-cm straight line. The left end of the line represented "no fatigue", and the right end of the line represented "most fatigue". At the time of assessment, the patient indicated her degree of fatigue on the straight line and the researcher assessed the degree of fatigue in the patient by measuring the distance from the left edge to the point where the patient marked. VAS has been extensively used for the assessment of various feelings or emotions in previous studies and has been found to be reliable and valid.[18,19]

Symptom Distress Scale (SDS)

We used a Chinese version of the SDS developed by McCorkle and Young and modified by Lai.[20] The

SDS assesses the degree of uncomfortable complications in patients receiving chemotherapy. Twenty-two symptoms are addressed in the SDS, including nausea and vomiting, a change in appetite, insomnia, pain, fatigue, a change in bowel habits, dysuria, dyspnea, cough, abdominal distension, dry mouth, sore throat, ulcer, irritability, unstable emotions, a change in appearance, bleeding, fever and chillness, numbness, chest tightness, and gastric burning sensations. The symptoms were recorded on a scale of 1 (no complications) to 5 (very serious complications). The internal consistency of the original SDS was 0.83, with a Cronbach's α of 0.78. The Cronbach's α of the Chinese version as modified by Lai was 0.91.[20]

Actigraphy

Actiwatch is an activity monitor, designed for long-term monitoring of gross motor activity in human subjects.[13–15] It contains an accelerometer that is capable of sensing any motion with a minimal resultant force of 0.01 g. It is necessary to load a series of commands into the activity monitor prior to data collection. These settings lay in sampling parameters such as start time and date, and the period of time between samples known as the epoch length. Other settings include an identification string, gender and age data for the subject. Once the settings have been made, the activity monitor is ready to be placed on the subject. After data collection has been completed, the stored activity data are downloaded to a PC for analysis and permanent storage. All communication with Actiwatch is accomplished through an Actiwatch reader that is connected to a PC. Actiwatch Sleep Analysis (Cambridge Neurotechnology Ltd), a Microsoft Windows version software, is programmed for the transformation and analysis of sleep data acquired from Actiwatch. These data include sleep latency, total sleep time, and sleep efficiency through records of activity associated with the record of the sleep logs.

Studies have shown actigraphy to be a valid and reliable tool for measuring activity and sleep in a variety of healthy and sick populations.[3,13] Although actigraphy is a sensitive noninvasive tool that is easy to use, some researchers have found that actigraphy overestimated sleep quality such as total sleep time and sleep efficiency, and recommend that subjective data should be used as an adjunct to actigraphic data to assess sleep quality in order to increase accuracy.[11,14]

Sleep logs

Sleep logs were used to record related sleep information of the participants, including time to bed, time to wake up, total sleep time, sleep latency and sleep quality by self-report. Sleep logs have been shown to be valid and useful in previous studies of sleep-related clinical problems.[12,21] The Chinese version of the sleep log used in this study was a product issued by the International Foundation for Mental Health and Neurosciences in 2001.[15] We also asked participants to make a note in their sleep logs when they removed or put on the Actiwatch. Sleep logs provided information to assist in the analysis of actigraphy data and in the analysis of subjective sleep quality from patients' self-reports.

Epworth Sleepiness Scale (ESS)

Johns developed the ESS in 1991.[22] It assesses the individual's degree of daytime sleepiness during eight different phases of daily life. Each question is measured on a 0–3 point scale scored as follows: 0 = no chance of dozing; 1 = slight chance of dozing; 2 = moderate chance of dozing; 3 = high chance of dozing. The possible score on the ESS ranges from 0 to 24. Scores exceeding 6 points indicate slight sleepiness. Scores exceeding 10 points indicate moderate sleepiness and scores exceeding 16 points indicate high levels of sleepiness. The higher the score, the more likely the patient is to fall asleep or to suffer from sleeping problems.[13,23]

Data collection and analysis

All participants gave informed consent before their entry into the study. Questionnaires including relevant demographic information and the HADS, sleep logs, and FVAS were first administered to each patient. Then patients were trained to maintain the HADS, sleep logs, and FVAS data. They were also trained to use the Actiwatch. Actiwatch Sleep soft-

ware was used to compute the total sleep time, sleep efficiency, number of awakenings during sleep and total time spent awake. Descriptive statistical analyses, Spearman's rank-order correlation, Mann-Whitney U test, and the Wilcoxon signed-rank test were performed using SPSS for Windows version 10.0 (SPSS Inc, Chicago, IL, USA).

Results

Sixteen patients met the research criteria and were included in the study. Their mean age was 45 years (range, 29–59 years); 50% of patients were college graduates, 43.8% were unemployed, and 75% were married. Regular menstruation was reported by 62.5% of patients (although none reported menstruation at the time of data collection). Seven patients received a 21-day cycle CEF regimen, with the drugs injected on day 1. Nine patients received CMF chemotherapy, of whom seven were on a 28-day cycle with injections on days 1 and 8, and the other two were on a 21-day cycle with injections on day 1 (Table 1).

Table 1. Characteristics of 16 patients with breast cancer

Variable	*n* (%)
Age	
≤ 40 yr	6 (37.5)
41–50 yr	5 (31.3)
51–65 yr	5 (31.3)
Education	
≤ Junior high school	2 (12.5)
Senior high school	3 (18.8)
University	8 (50.0)
Graduated	3 (18.8)
Marital status	
Single	4 (25.0)
Married	12 (75.0)
Menstruation	
Menopause	6 (37.5)
Normal	10 (62.5)
Chemotherapy regimen	
CEF	7 (43.8)
CMF	9 (56.2)

CEF = cyclophosphamide, epirubicin, fluorouracil; CMF = cyclophosphamide, methotrexate, fluorouracil.

Psychologic and physical distress

During the active phase of chemotherapy, the mean HADS score for anxiety was 7.81 ± 3.76, indicating increased anxiety in patients. The mean FVAS score was 4 ± 2, indicating a mild degree of fatigue. Comparison of mean SDS scores between the active and recovery phases of chemotherapy using the Wilcoxon signed-rank test revealed a significant difference ($Z = -3.260$, $p < 0.01$) (Table 2). A greater degree of symptom distress was reported during the active phase than during the recovery phase. The top three causes of symptom distress during the active phase were change in appearance (2.8 ± 1.1), fatigue (2.6 ± 0.9), and reduced appetite accompanied by nausea (2.6 ± 1.2). The top three causes of symptom distress during the recovery phase were fatigue (2.2 ± 1.0), change in appearance (2.0 ± 1.0), and the feeling of thirst (1.9 ± 0.6).

Sleep quality

Mean sleep latency during the active phase was 35.1 ± 30.5 minutes as measured by sleep logs, and 22.7 ± 24.6 minutes as measured by Actiwatch. The number of awakenings during the sleeping period as measured by sleep logs was 2.2 ± 1.6. The total time spent awake during the sleeping period as measured by Actiwatch was 47.8 ± 26.1 minutes. Sleep efficiency during the active phase as measured by actigraphy was 82.1 ± 9.4%. The ESS score for daytime drowsiness during the active phase was 6 ± 3.5, indicative of a light doze. In contrast, patients had a lower ESS score of 4.3 ± 3.6 during the recovery phase (Table 2). These results indicate that patients suffered from daytime drowsiness during the active phase but not during the recovery phase ($Z = -1.97$, $p < 0.05$, Wilcoxon signed-rank test). The degree of symptom distress correlated positively with the scores of daytime sleepiness ($r = 0.787$, $p < 0.01$, Spearman's rank correlation), i.e. greater distress levels were associated with greater daytime drowsiness. The sleep

Table 2. Psychologic and physical distress and sleep quality in 16 patients with breast cancer during the active and recovery periods of the third cycle of chemotherapy

	Subjective (mean ± SD)			Objective (mean ± SD)	
	Active	Recovery	Z	Active	Recovery
Psychologic and physical distress					
Anxiety measured by HADS	7.8 ± 3.8	7.3 ± 3.4		–	–
Depression measured by HADS	4.8 ± 2.7	5.3 ± 3.3		–	–
Fatigue measured by FVAS	4 ± 2	3.6 ± 2		–	–
Symptom distress measured by SDS	39.8 ± 7.2	30.6 ± 5	–3.26*	–	–
Sleep quality					
Actual sleep time (min)	446.5 ± 69.1	466.1 ± 67.5		395.1 ± 73.8	391.2 ± 72.9
Sleep latency (min)	35.1 ± 30.5	23.1 ± 18.3		22.7 ± 24.6	23.6 ± 26.2
Number of awakenings	2.2 ± 1.6	2 ± 1.0			
Total time awakened (min)				47.8 ± 26.1	56.4 ± 31.3
Sleep efficiency (%)	92.8 ± 5.2	95.3 ± 3.3		82.1 ± 9.4	79.9 ± 9.7
Daytime sleepiness	6 ± 3.5	4.3 ± 3.6	–1.97†	–	–
Subjective sleep quality	2.8 ± 0.5	3.3 ± 0.7	–2.02†	–	–

**p < 0.01, †p < 0.05 (Wilcoxon signed-rank test). HADS = Hospital Anxiety and Depression Scale; FVAS = Fatigue Visual Analogue Scale; SDS = System Distress Scale.*

quality scale score during the active phase was 2.8 ± 0.5, indicating that most patients considered their sleep quality to be between "common" and "bad". Patients enjoyed better sleep quality during the recovery phase than during the active phase ($Z = -2.02$, $p < 0.05$, Wilcoxon signed-rank test).

Discussion

The study found that during the active phase of chemotherapy, when side effects are acute, patients demonstrated a longer period of subjective sleep latency than after recovery from treatment. A similar observation that more than half of patients had a longer period of sleep latency than healthy controls has been reported.[5] Cohen et al further suggested that long sleep latency indicated poor sleep quality during the active phase of chemotherapy.[24] We also found that the number of sleep interruptions and waking hours increased during the active period of chemotherapy. Patients woke more often at night during the active phase of chemotherapy.[5] These findings confirm that chemotherapy increases the number of sleep interruptions during the active period.

The sleep efficiency rate of 82.1% as measured by the Actiwatch during the active phase of chemotherapy in this study is indicative of decreased sleep efficiency. This is consistent with another report that half of the patients had a sleep efficiency rate of less than the normal 85% during active chemotherapy.[5]

In this study, daytime drowsiness was more common during the active phase than during the recovery phase of chemotherapy. This result is consistent with the study of Berger and Farr, who found that patients demonstrated a low degree of activity in the daytime and took frequent naps during the active phase of chemotherapy.[10] These findings show that chemotherapy affects patients' daytime function by causing drowsiness. Chemotherapy is, thus, associated with poor sleep quality and may also have psychologic impacts associated with daytime drowsiness, as previously reported by Piper.[3]

We found that sleep quality was negatively affected during the active phase of chemotherapy. Patients enjoyed better sleep quality during the recovery phase than during the active phase. Further research is needed to investigate the effects of different phases and regimens of chemotherapy. The results of such studies should be used to de-

sign effective strategies to alleviate these adverse effects.

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